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Lab-on-Chip Silicon nanowire biosensors for biomedical applications

Lean G. Pedersen, Azeem Zulfiqar, Andrea Pfreundt, Lars Andresen, Winnie E. Svendsen

Introduction

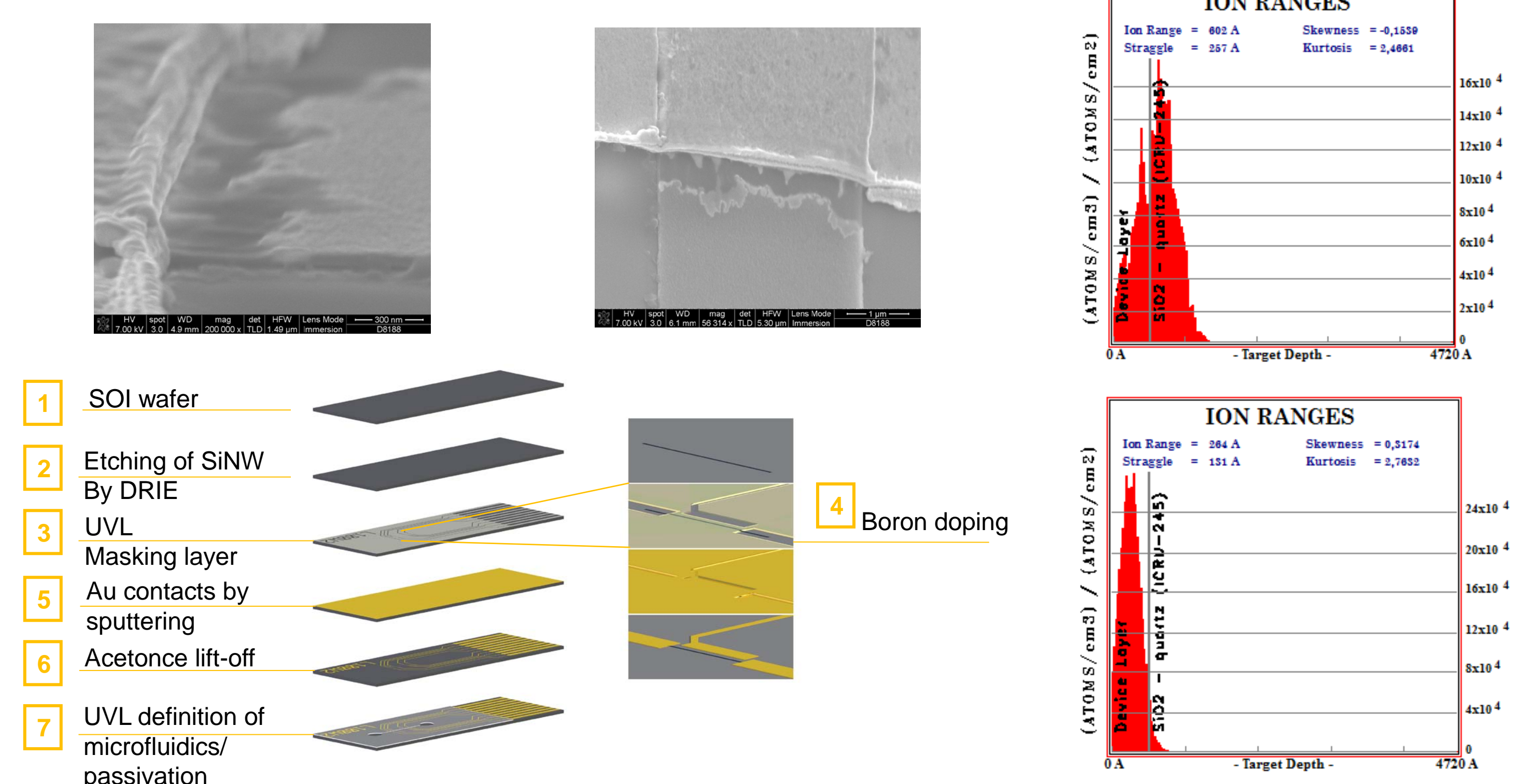
Low-cost point of care medical diagnostic methods are of crucial importance for the future health care system. Lab-on-chip (LOC) systems with Silicon nanowires (SiNW) in a Field-effect transistor (FET) setup can be used as biosensors. SiNW sensors can be highly sensitive and used in a variety of setups, making this material an excellent candidate for biosensor devices. SiNWs can be functionalized with e.g. antibodies, to ensure sensing specificity for a wide range of biological markers. This allows for detection of small amounts of antigens for diagnosis of diseases already in an early stage allowing for development of personalized therapy.

Our aim is to develop a reliable and reproducible diagnostic tool. For this purpose it is essential to understand the details of the effects which lead to the high sensitivity that is achievable with these kind of devices.

Fabrication

Our fabrication process consist of standard cleanroom procedures. We have investigated different processes to increase the yield of biosensors.

- Ion-implantation of heavier atoms with high energy provides an advantage over lighter atoms with low energy for shallow doping.
- As an alternative, Spin-on-glass (SOG) diffusion of dopants creates less damage and is cheaper than ion-implantation.
- Rapid Thermal Annealing (RTA) is a fast alternative to ordinary annealing which enables better control of the diffusion process.
- Sputtering of the metal connections provides more stable electrical connections as compared to evaporation.

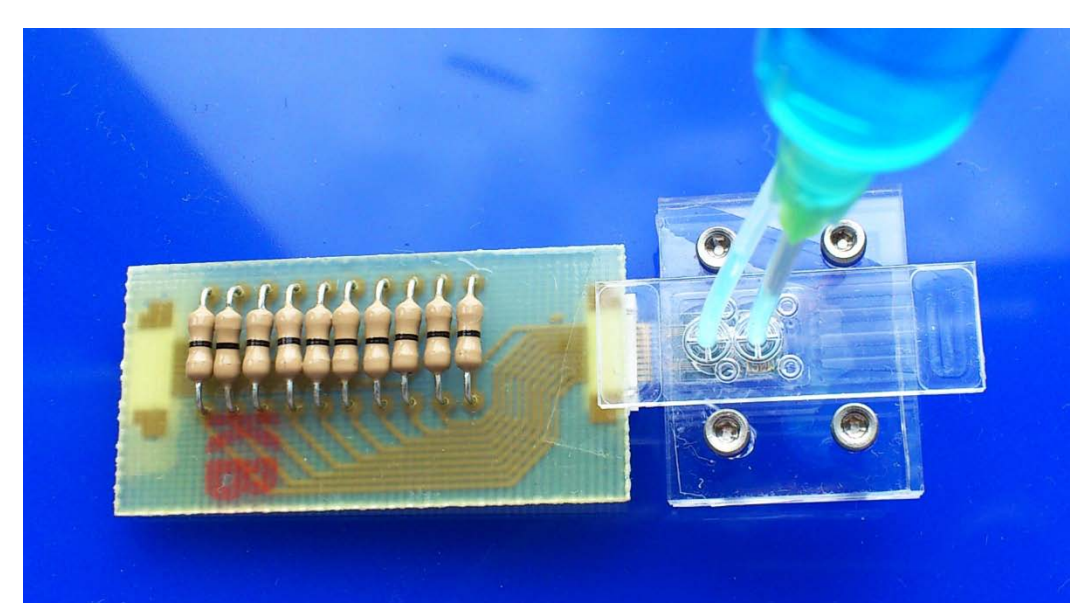
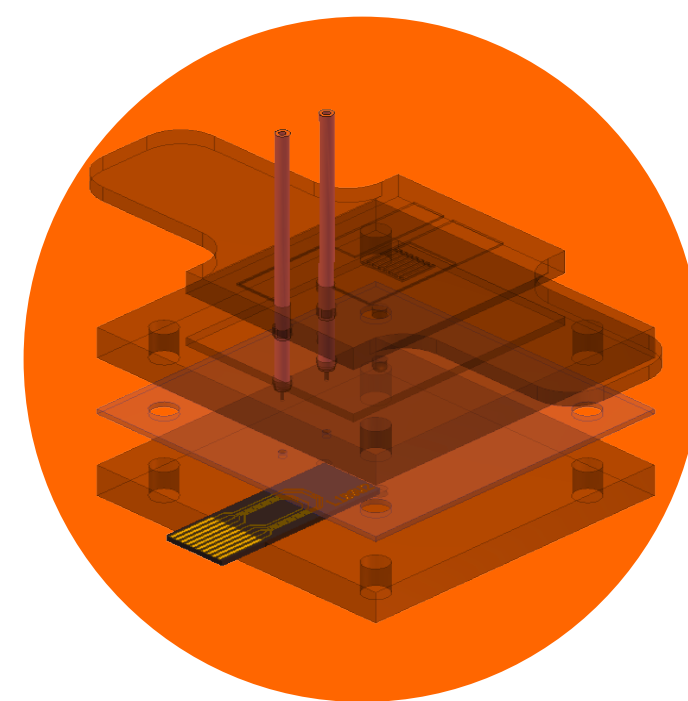


Microfluidics

Our microfluidic interface enables automation of functionalization and control of the measurement environment.

We have investigated different passivation layers that can be integrated with microfluidic devices.

- As an alternative to SU-8, polyimide is being investigated for passivation and fluidics.
- The SiNW chip is contained in a PDMS/PMMA microfluidic flowcell to provide an interface for easy functionalization.
- Microfluidic interconnections have been improved in order to facilitate repeated usage.

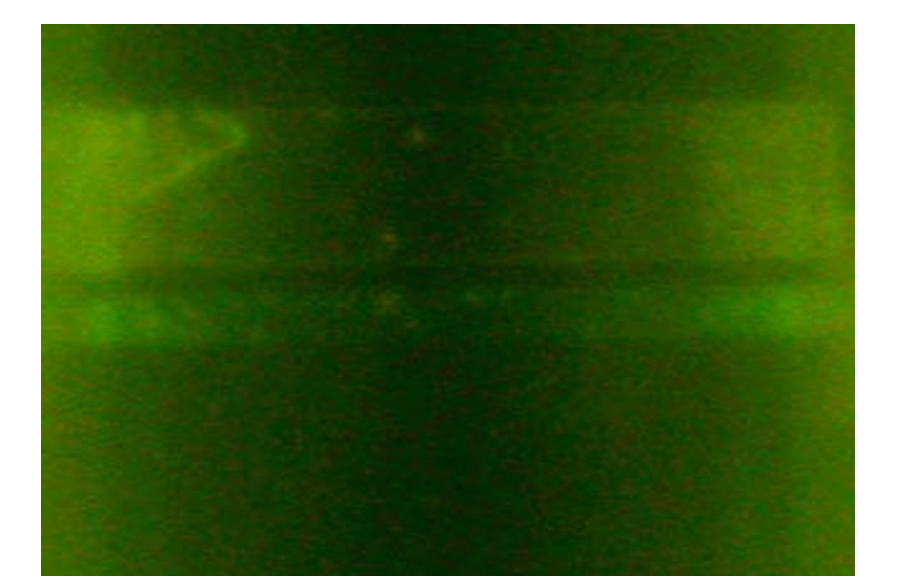
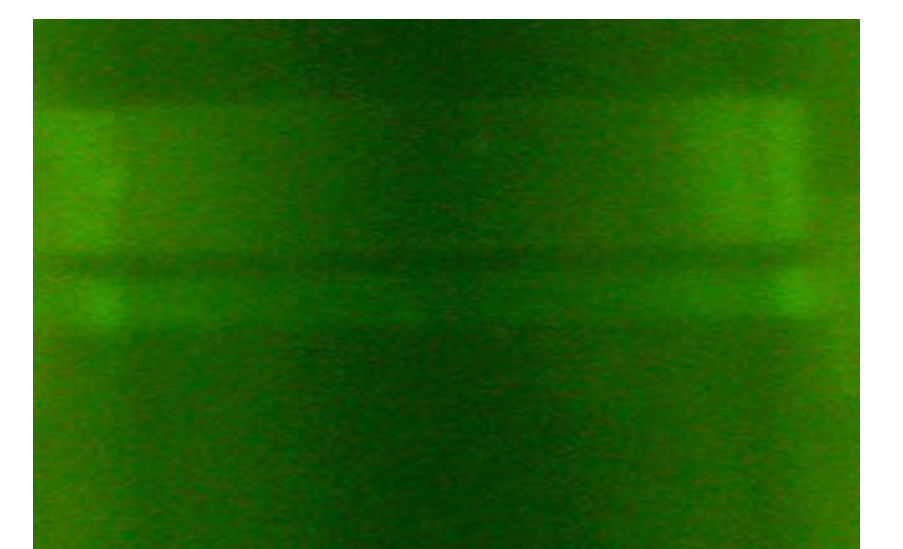
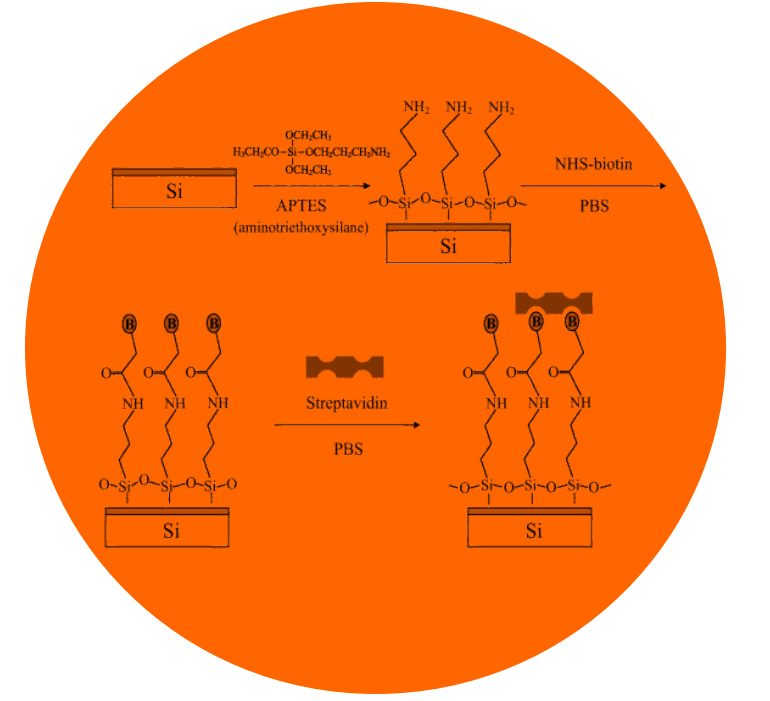


Functionalization

Functionalization of NW's are the crucial step for specific detection of biomolecules.

Different immobilization strategies have been investigated and optimized using fluorescent markers and impedance measurements.

- Fluorescent protein has been immobilized on a SiNW.
- Proof of concept of: A complementary DNA strand hybridized to a immobilized DNA on the NW is performed on another type of chip.
- Regeneration of the functionalization layer has been shown successfully.



Conclusion

Investigation and optimization of the different steps to increase the yield of reproducible, sensitive, and robust silicon nanowire biosensors in a lab-on-a-chip system for detection of different diseases is a still ongoing process.

Though the procedure consist of standard processes in a cleanroom, it is not fully understood how every step affects the final product. Therefore we are performing thorough investigations on every step which covers most encountered issues such as stress, poor doping levels, leaking fluidic systems, low yield, low sensitivity, connection, and signal.

Our preliminary data shows that:

- The ion-implantation should be done by BF₄ at high energy instead of boron at low energy.
- The fabrication of PMMA and PDMS microfluidic systems is less time consuming and is applicable for other systems.
- Sputtered gold electrodes are more stable and have better coverage than evaporated gold electrodes.
- Fluorescent DNA can be immobilized on NW's. The proof of concept of is made by Kasper B. Frøhling, however, the experiment was performed on a different chip.